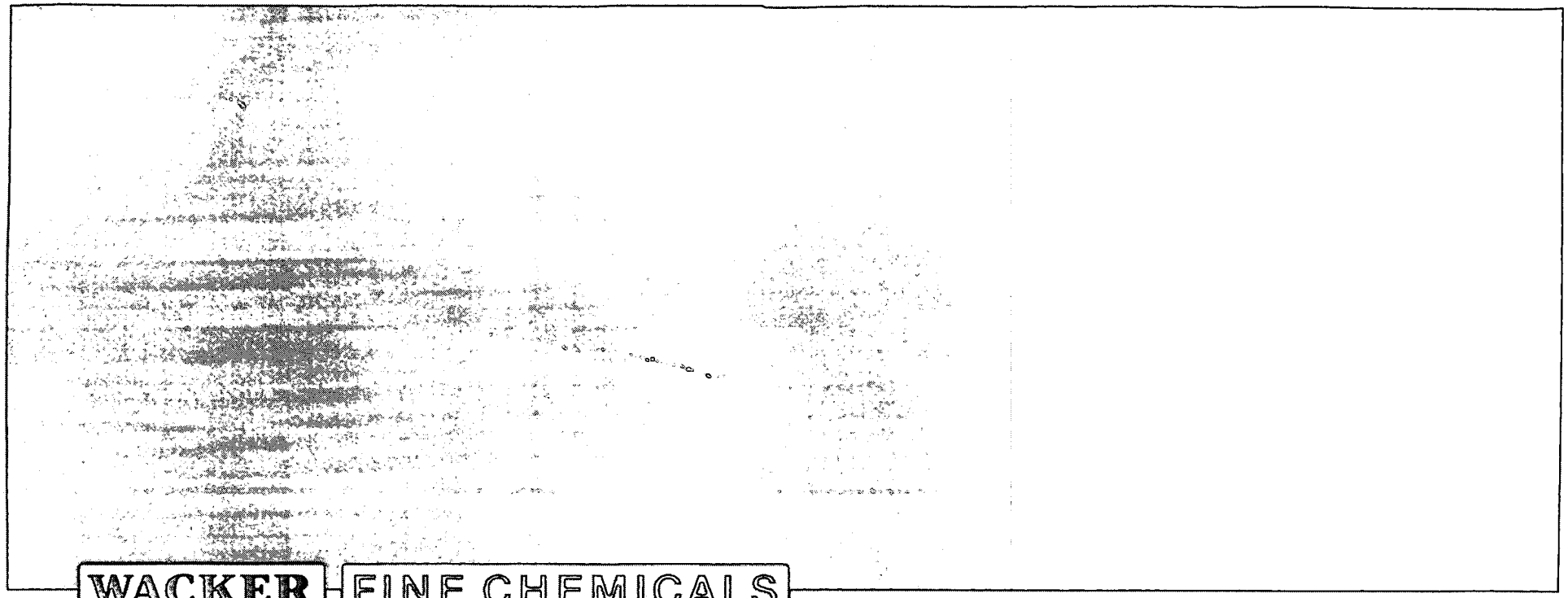


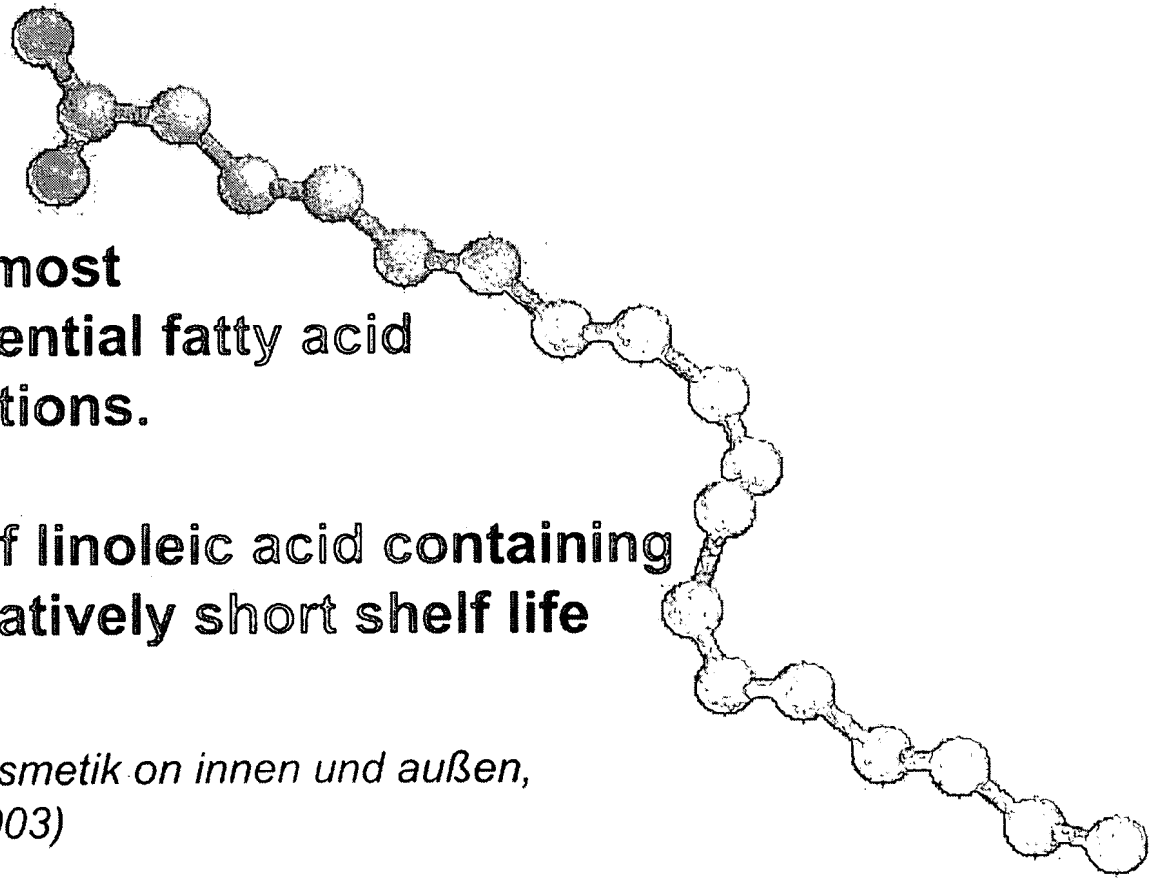
WACKER FINE CHEMICALS

# CYCLODEXTRINS ANOTHER TOOL FOR ENCAPSULATION OF LINOLEIC ACID

Regiert Marlies, Kupka Michaela, Sigl Harald, F-I-P, March 2005

CREATING TOMORROW'S SOLUTIONS

# LINOLEIC ACID, $C_{17}H_{31}COOH$, E.G. (Z,Z)-9,12-OCTADECADIENOIC ACID

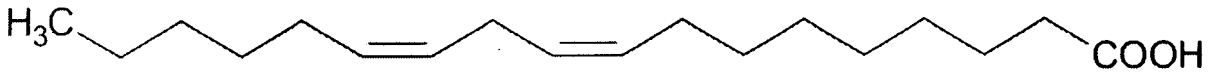


**Linoleic acid is the most frequently used essential fatty acid in cosmetic formulations.**

**One disadvantage of linoleic acid containing oils is there comparatively short shelf life**

*(Essenzielle Fettsäuren - Kosmetik on innen und außen, Dr. Hans Lautenschläger, 2003)*

# FUNCTION, PHYSIOLOGICAL EFFECTS




- Belongs to the group of omega-6 fatty acids
- It cannot be synthesized by animals
- Linoleic acid is incorporated in the skin to the most important barrier-active "ceramide I"
  *(Essenzielle Fettsäuren - Kosmetik von innen und außen, Dr. Hans Lautenschläger, 2003)*
- Is essential for the human body

# FUNCTION, PHYSIOLOGICAL EFFECTS

- Is important for the synthesis of eicosanoids, which have a regulatory action in various tissues

  *(Technical Information BASF, „products for the food and pharmaceutical industry", 2002)*

- A lack of linoleic acid in the skin has e.g. the effect of:
  - barrier disruption of the skin
  - a higher rate of the trans-epidermal water-loss
  - the skin becomes dry, scale and gets a unhealthy colour

- Acts both as a concentrated energy carrier and as a starting material for the synthesis of arachidonic acid (important component of cell membranes)

  *(Technical Information BASF, „products for the food and pharmaceutical industry", 2002)*

# FUNCTION, PHYSIOLOGICAL EFFECTS

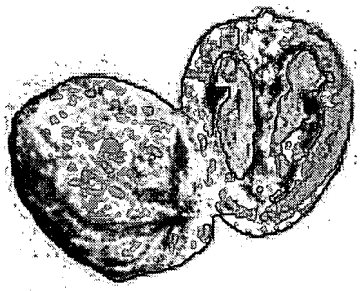
- Requirements / intake recommendations:
  the adult requirement of linoleic acid is 8 – 10g per day
- There is an increased requirement for essential fatty acids after severe accidents and in certain diseases

# PROPERTIES AND OCCURRENCE

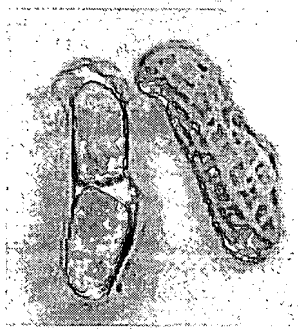
- Is a colorless to straw colored liquid
- Insoluble in water, soluble in oil and fats
- Is the most common polyunsaturated fatty acid
- Linoleic acid also may convert to a isomeric unsaturated conjugated fatty-acid
- It is easily oxidized by air to peroxides that have undesirable biological effects
- Vegetable oils become rancid when exposed to air at room-temperature and can seriously spoil the taste, odor and stability of food products
- It is found in nature in plants and animal tissues

# OCCURRENCE

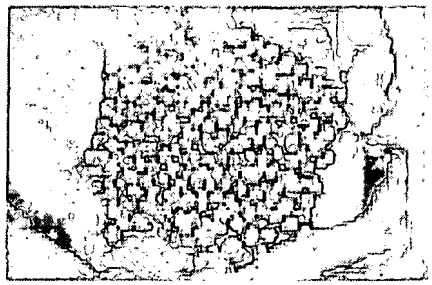
walnut



peanut

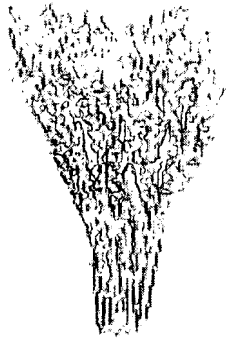


soya



seeds of sunflower

corn



# CONVERSION FROM LIQUID TO SOLID COMPLEX

**Left:**

pure linoleic acid

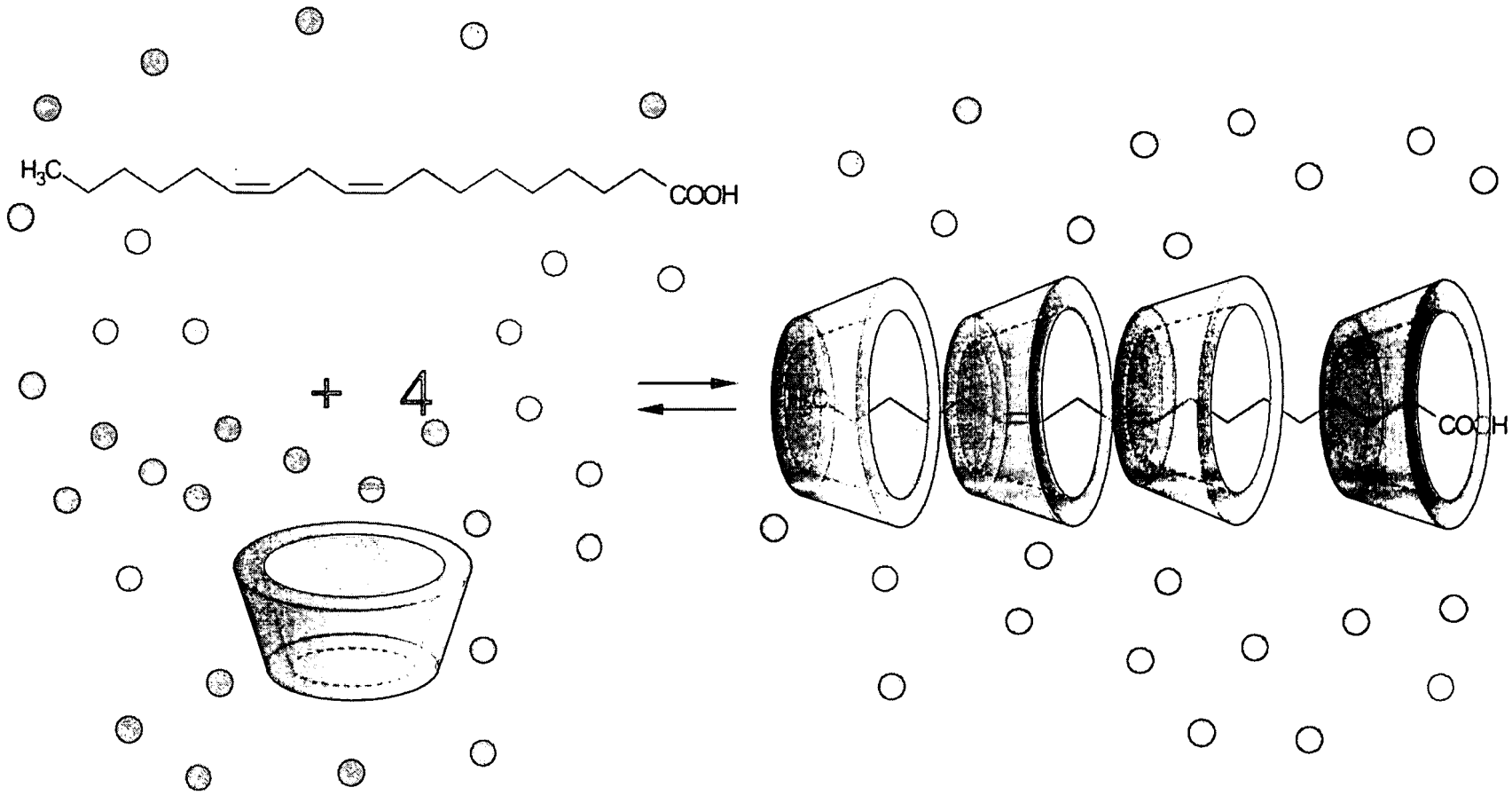
**Right:**

CAVAMAX®W6/LINOLEIC ACID-COMPLEX

# APPLICATION

- As component in cosmetic formulations like
  - emulsion, cream
  - gel
  - lip-balm
- Colour cosmetic, like lip-stick
  - face powder
  - eye shadow
  - face mask
- As component in derma products
  linoleic acid helps to cure
  - skin disease
  - sun burn
  - burns
  - akne vulgaris

# SCHEMATIC REPRESENTATION OF AN INCLUSION COMPLEX FORMATION BETWEEN CYCLODEXTRIN AND LINOLEIC ACID



# CAVAMAX® W6/LINOLEIC ACID-COMPLEX, CHARACTERISTICS

| | CAVAMAX®W6-Complex |
|---|---|
| appearance: | white granulate/powder |
| active content: | min. 7.5 % (NMR, GC) |
| water content: | max. 14% |
| INCI names | cyclodextrin/linoleic acid |
| patent pending | DE10253042.4-4; EP03026137.4; JP 2003-385675; KR 2003-0077579 |

# BENEFITS OF CAVAMAX® W6/ LINOLEIC ACID -COMPLEXES BY APPLICATION IN FORMULATIONS

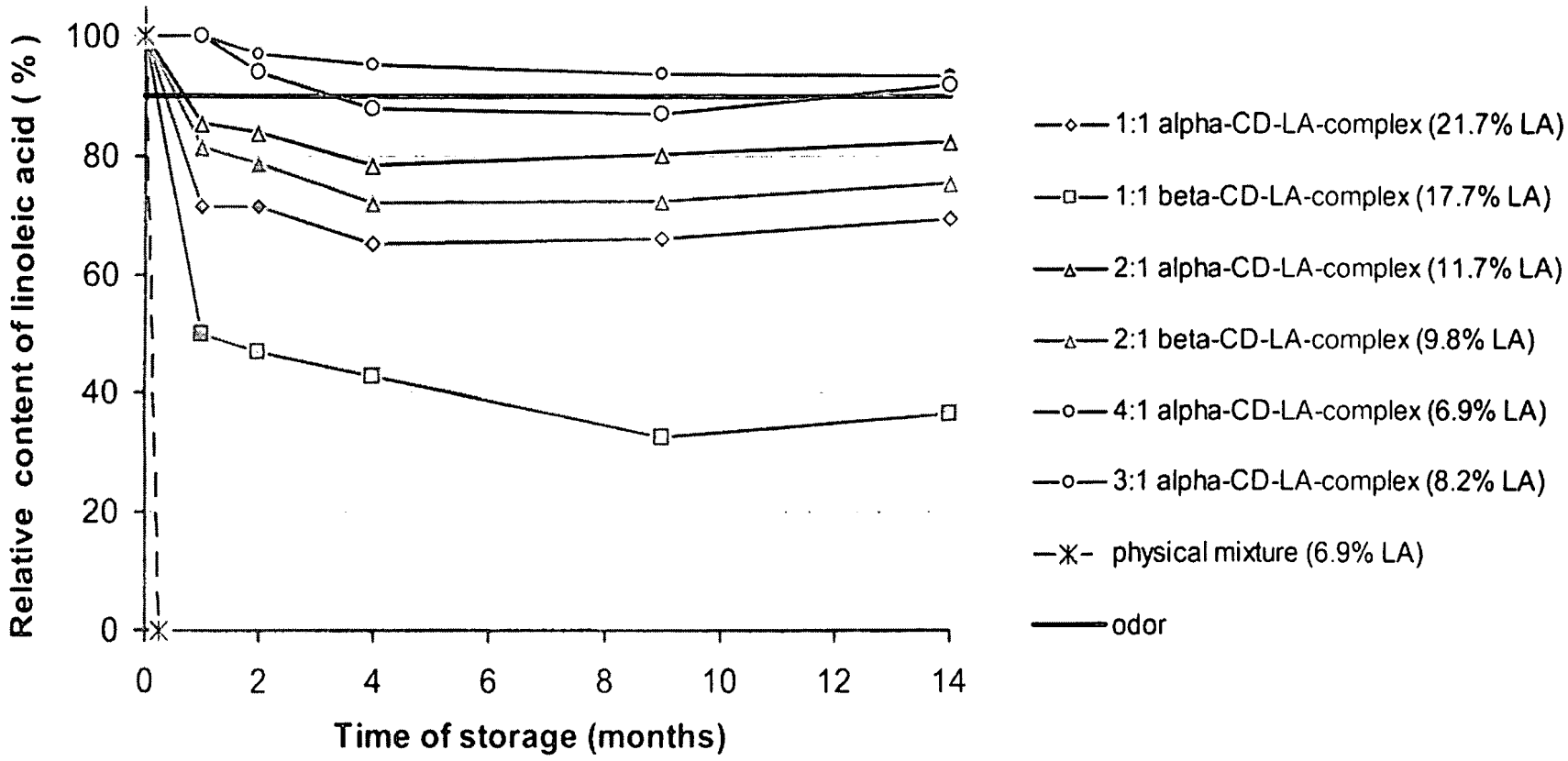
- Improved stability of linoleic acid e.g. oxygen, UV-A and UV-B and temperature
- Controlled release
- No rancidness in finished products e.g. during application
- No need of a stabiliser in cosmetic formulations
- Preparation of cosmetic formulations is even possible at higher temperatures
- Easy handling

# BENEFITS OF CAVAMAX® W6/ LINOLEIC ACID-COMPLEXES BY APPLICATION IN FORMULATIONS

- Stable dispersion/emulsion
- Increase of texture of emulsions
- Efficient depot system
- Positive costs/benefit-factor
- Recommended dosage:
  0.5 - 15% of CAVAMAX®W6/LINOLEIC ACID-COMPLEX
- In food products: improved taste and odor stability

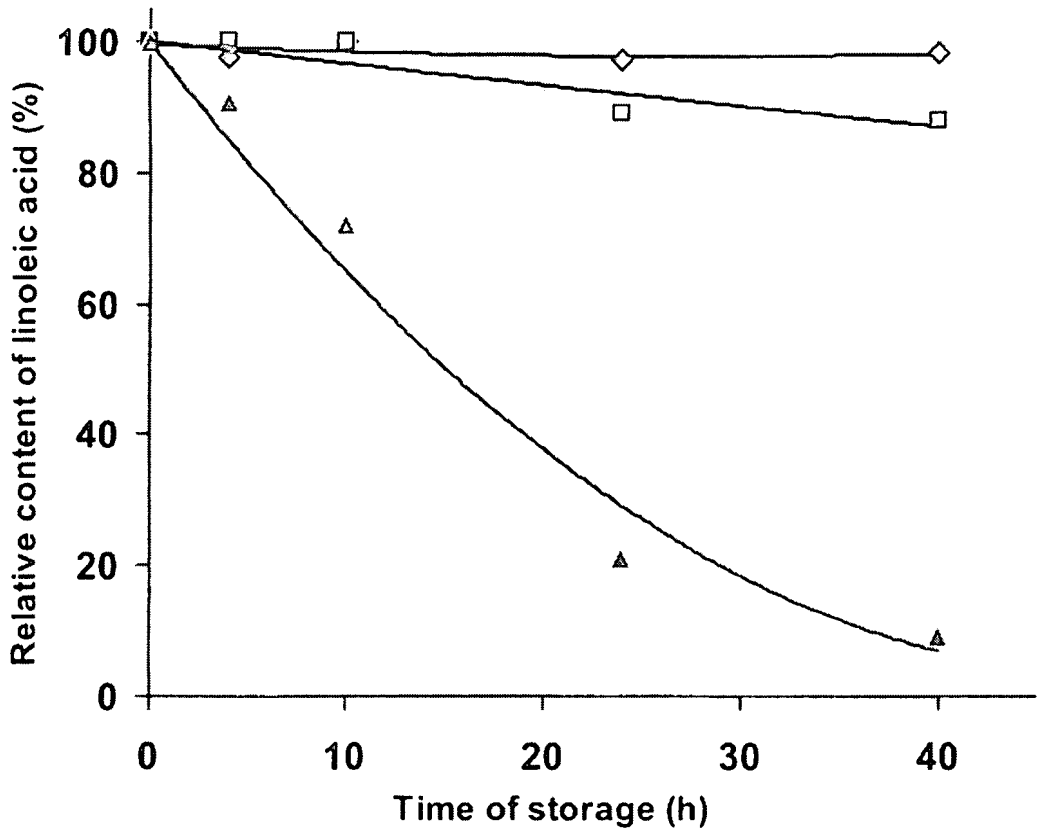
# THERMOSTABILITY OF CAVAMAX®/LINOLEIC ACID-COMPLEXES WITH VARIOUS MOLAR RATIO OF ACTIVE AT 45°C

Stability at 45°C, stored in open vessels (90 mm diameter, 3 mm layer)



# UV-STABILITY OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID IN GEL

Stability in Sun Screen Softgel (1.0 % linoleic acid. "suntest" UV-A and UV-B, 45 °C)



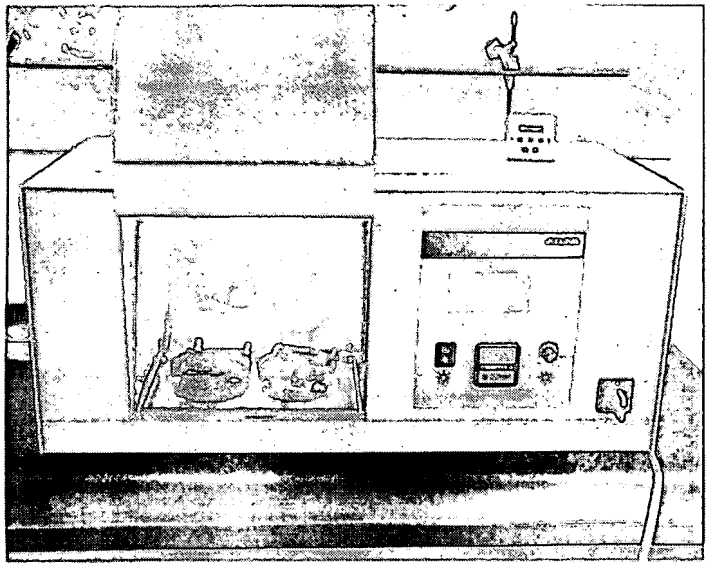

◇ Softgel + 4:1-alpha-cyclodextrin-linoleic acid-complex

□ Softel + 3:1-alpha-cyclodextrin-linoleic acid-complex

△ Softgel + linoleic acid uncomplexed

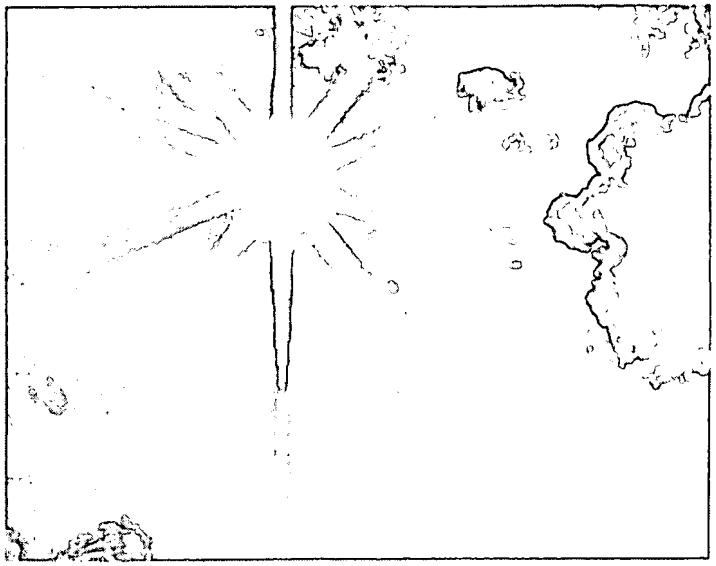
# UV-STABILITY TEST IN SUN-TEST DEVICE: COMPARISON

**SUN-Test device**



max. irradiation/day = 66 MJ/m²

**"Sun-Bathing"**



irradiation/day (middle europe) = 5.7 MJ/m²

ratio (time lapse factor) =

**11** : **1**

# UV-A AND UV-B STABILITY TEST IN SUN-TEST EQUIPMENT

**Method**

| | |
|---|---|
| Equipment | SUNTEST CPS from ATLAS |
| Radiation-source | Xenon-Lampe |
| Optical filter | Solar Standard<br>(filter referring to **COLIPA*** and DIN 67501) |
| Air cooled sample room | max. determined inside-temperature = 45°C |
| Maximum radiance | E (300nm – 800nm) = 765W/m² |
| Constant controlling of the Irradiation | via photodiode |

*(source: ATLAS-Material Testing Solutions)*

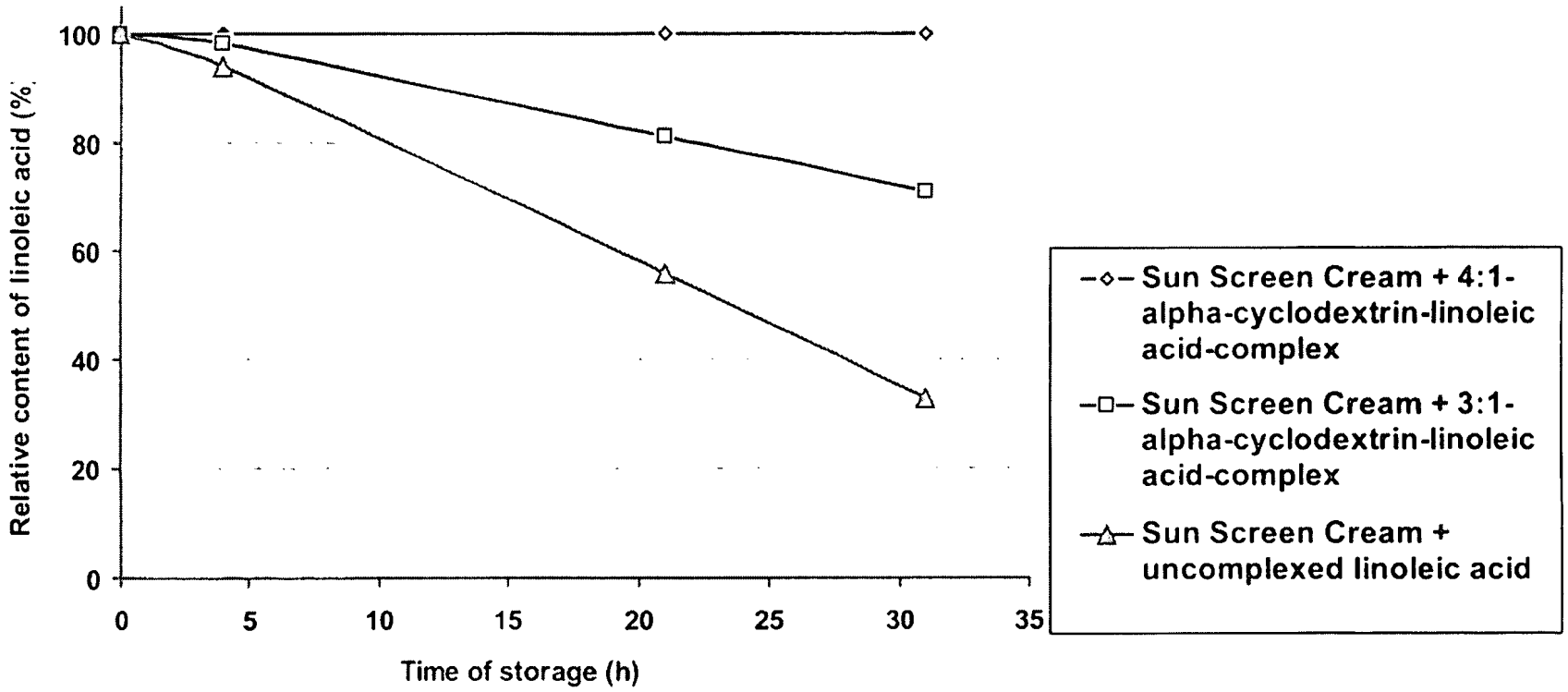
**Sample preparation**

Solid substance like cyclodextrin-complex
3 – 4 g substance between 2 layers of glass 10 x 10 cm
(glass rim has to be covered with an adhesive tape )

Soft substance like creams und pastes
3 – 4 g in a PE-plastic bag 10 x 10 cm (melted rim)

# UV-STABILITY OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID IN CREAM

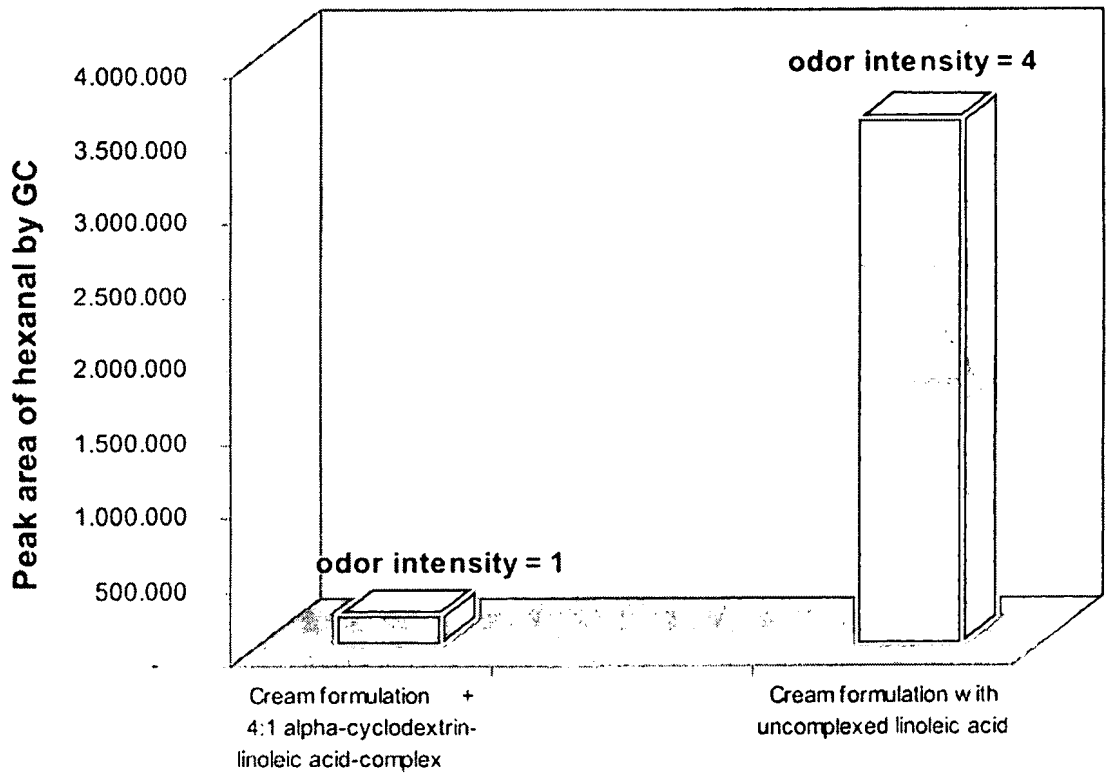
Stability in Sun Screen Cream
(1.0 % linoleic acid content, "suntest" UV-A and UV-B, 45 °C)



# LONG-TERM STABILITY OF 1% LINOLEIC ACID AS 4:1-ALPHA-CD/LA-COMPLEX AND UNCOMPLEXED IN CREAM

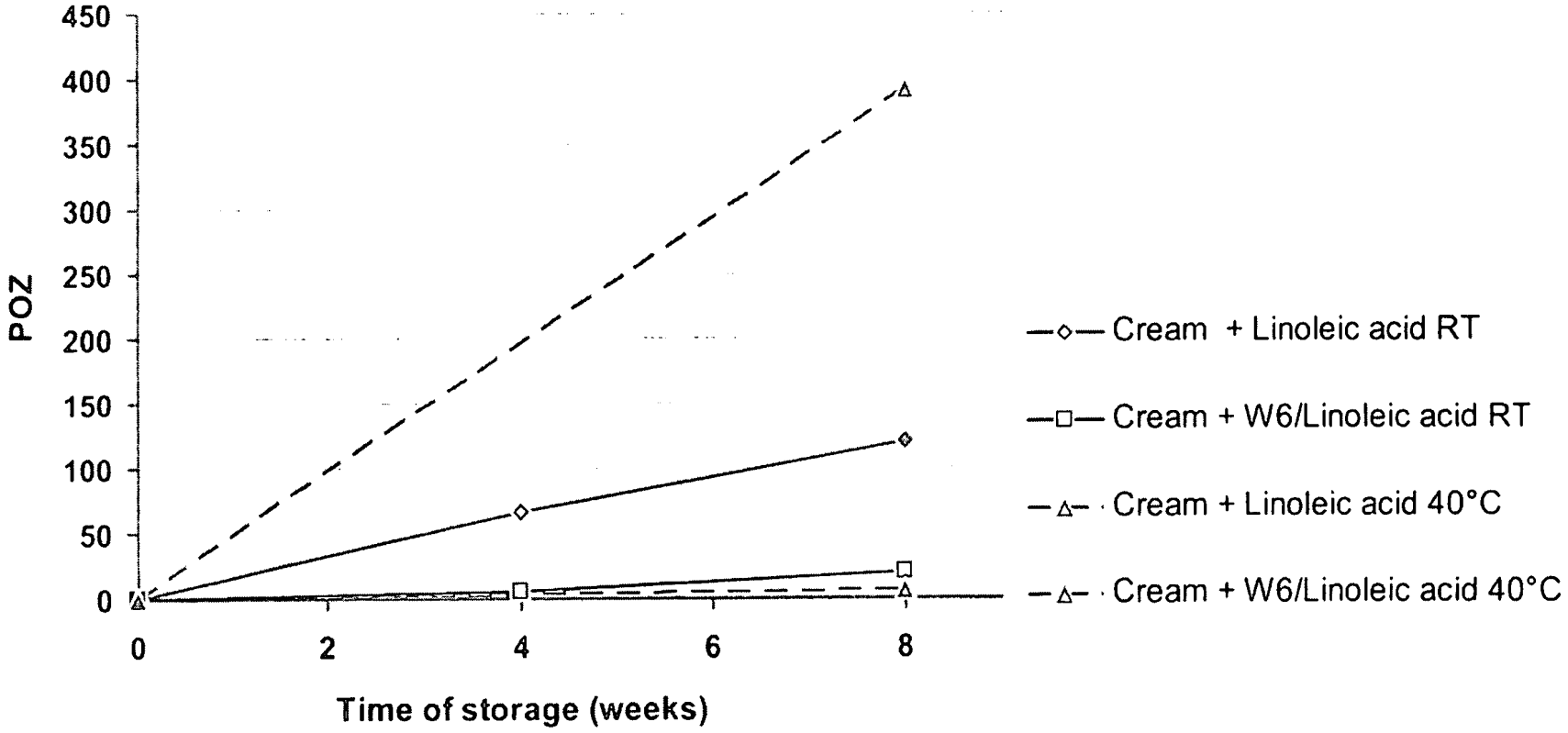
at room temperature after 12 months storage.

Sensory- and SPME/GC-Analysis of deteriorated linoleic acid e.g. as Hexanal



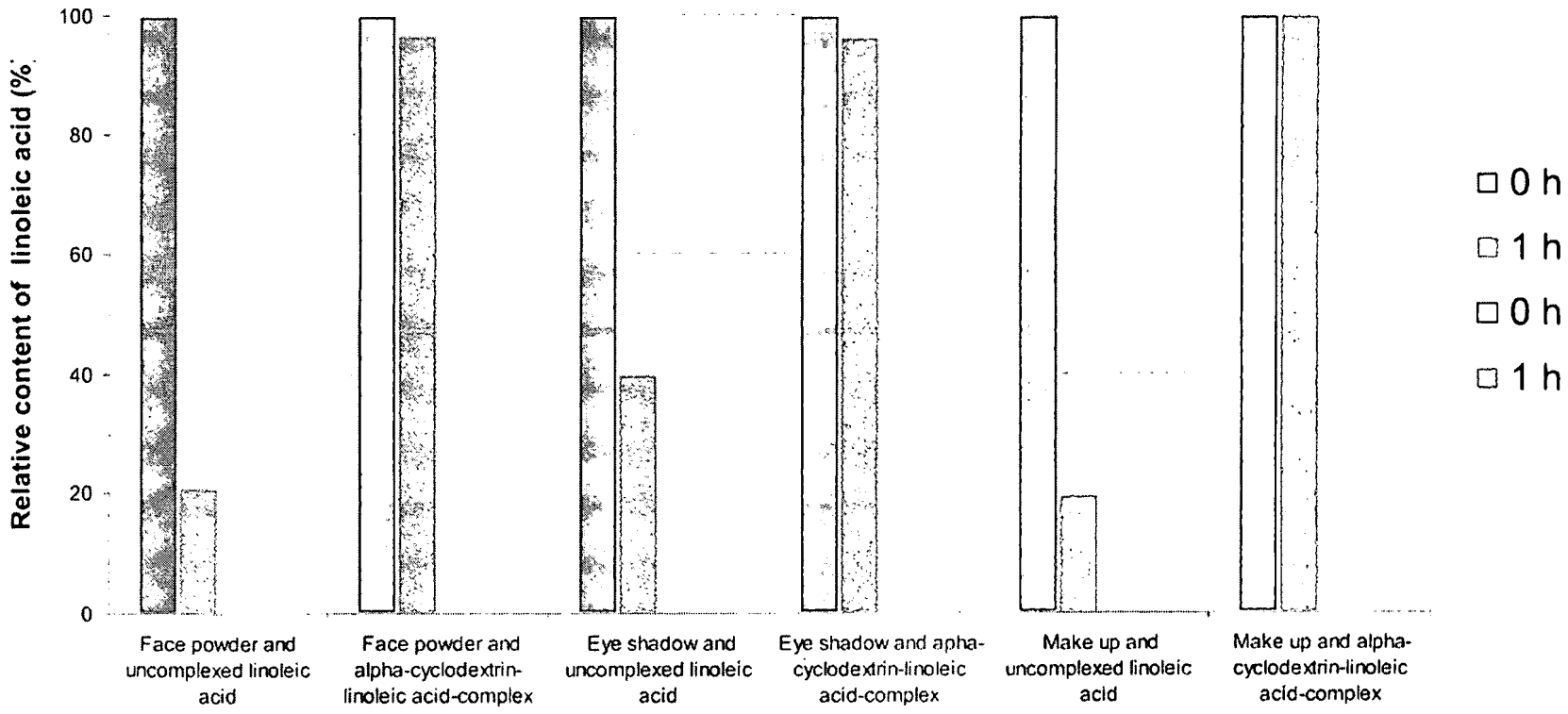
# DEGRADATION OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID BY PEROXIDE VALUE

Instability in Cream W/O stored at different temperatures, (1.0% linoleic acid content) determined by peroxide value



# LIGHT-STABILITY OF 1% LINOLEIC ACID AS 4:1-ALPHA-CD/LA-COMPLEX AND UNCOMPLEXED IN COLOR-COSMETICS

"Sun-Test" UV-A and UV-B at 45 °C; GC-Analysis of Linoleic Acid-Content



# DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

## Analytical Method

| | |
|---|---|
| Principle of the Method: | Silylation by MSHFBA, GC-Direct Injection, Internal Standard |
| Name of the analyte : | Linoleic Acid |
| Retention times (min) : | Analyte (Linoleic Acid) 8,71 |
| | Int.Std. (Eicosanoic Acid) 10,21 |
| Sample name, matrix: | Cyclodextrin or Cosmetic Products |
| Solvent: | Solvent-Mix 80 % v/v Pyridine + 20 % v/v THF |
| Quantitation - method : | Internal Standard ISTD |
| INTERNAL Standard: | Eicosanoic Acid (C20) CAS - NR.: [530-30-9] |

## Internal Standard solution

Prepare a concentrated (e.g. about 1100 ppm) stock solution of Eicosanoic Acid in the solvent mix. Add a small volume (about 0.8 g) of that stock solution to (about 5g) of the Silylating Reagent MSHFBA to get a ISTD-working solution:
150 ppm ISTD in (MSHFBA > 95 %, < 5% solvent mix).

# DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

**Sample preparation:**

Dissolve the sample ( Cyclodextrin 0.1 %, Cosmetic Products 1 % ) in the solvent mix (rise in temperature, short ultrasonic agitation).

**Silylating Reaction:**

200 mg of the sample solution are diluted with 700 mg THF + 100 mg ISTD-working solution = 1000 mg reaction solution with 15 ppm ISTD. Heat the reaction mixture (70 °C, about 15 min) --- Alu Block Heater.

# DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

**Calibration Range:**

Analyte: 5 to 20 mg/kg solvent
ISTD: 15 mg/kg solvent

**Calibration solutions**:

Prepare solutions of linoleic acid and eicosanoic acid in the pyridine/THF-solvent mix separately and store them in a refrigerator (< 1 month, without silylation).
Dilute and mix the separate solutions to get >= 5 linoleic acid-calibration levels within the calibration range 5-20 ppm with constant 15 ppm ISTD-concentration for all levels.
Silylating Reaction:
Add 10 % (w / w) of the silylating reagent to the calibration solutions. Heat the calibration mixtures (70°C, about 15 min) --- Alu Block Heater.

**Reagents**:

THF p.A.
Pyridine
MSHFBA, N-Methyl-N-trimethylsilylheptafluorbutyramid (Macherey-Nagel)

# DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

## GC - Operating Conditions

| | | | | |
|---|---|---|---|---|
| Instrument: | Gaschromatograph HP 6890 equipped with FID and autosampler | | | |
| Column: | 30 m x 0. 32 mm ID fused silica capillary column | | | |
| Stationary phase: | HP-5 Methyl-Polysiloxan with 5 % Phenyl-Polysiloxan | | | |
| Film Thickness: | df = 0,23 µm | | | |
| Supplier : | Agilent | | | |
| Column temperature: | | | | |
| Temp. program : | Initial temp. | 60 °C | Initial Time | 1. 0 min |
| | Program Rate A | 30 °C / min | Program Rate B | - °C / min |
| | Final Temp. | 250 °C | Final Temp. | - °C |
| | Final Hold Time: | 7.0 min | Final Hold Time: | - min |
| | Analysis Time: | min | | |
| Carrier gas: | | Helium | | |
| Column Head Pressure: | | 117 kPa | | |
| Flow Rate: | | 1,5 ml / min | | |
| Electronic pressure control: | | Constant Pressure | | |
| Injection: | | Direct Injection with autosampler HP 7673 A, Splitless mode | | |

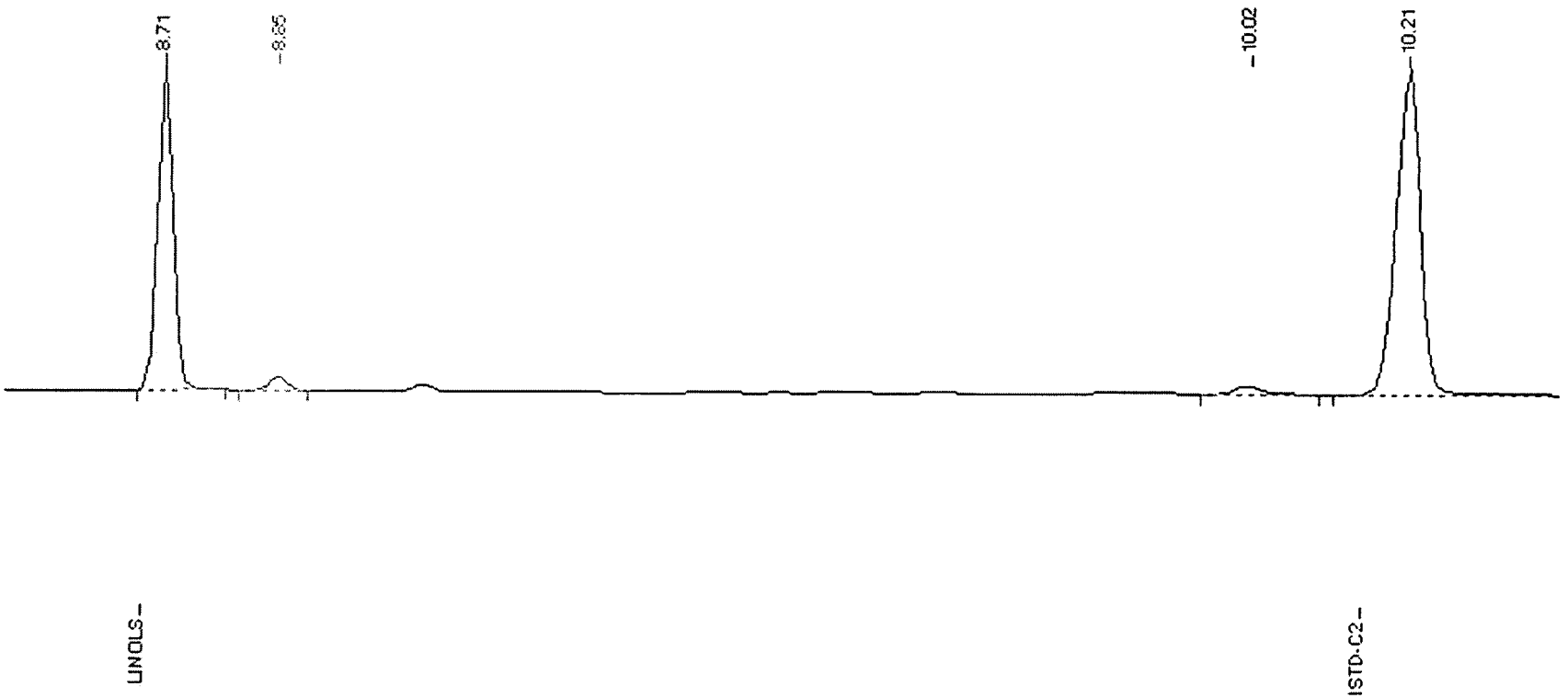
# DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

| | | |
|---|---|---|
| Inject samples: | Silylation reaction mixture of the calibration solutions and of the sample solution, respectively. | |
| Injektionvolume (µL): | 1 | |
| Inlet: | Split/Splitless capillary inlet with EPC | |
| Temperature: | 300 °C | |
| Split Flow: | 100 ml / min | Purge B off 0 min<br>Purge B on 0,9 min |
| Septum Purge : | 3-5 ml / min | |
| Detector: | FID | Temperature 300°C |
| Hydrogen: | 40 ml/min | |
| Air : | 450 ml/min | |
| Make up gas: | Helium 29 ml/min | |
| Data acquisition and quantitation software: | PE Turbochrome | |
| Appendix: | Representative chromatogram | |
| Representative GC-Run: | Linoleic acid with Int. Standard Eicosanoic Acid after Silylation | |

# DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

**Representative GC-Run:**

Linoleic Acid with Internal Standard Eicosanoic Acid after Silylation



# PREPARATION OF A SUN SCREEN SOFT STICK WITH (0.30 W/W%) LINOLEIC ACID

| | Ingredients | INCI-Names | w/w | Supplier |
|---|---|---|---|---|
| A) | Vaseline | Petrolatum | 68,9% | |
| | Wacker Belsil® SDM 6022 | Stearoxy Dimethicone, Dimethicone | 25,0% | Wacker-Chemie AG |
| B) | CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linleic acid) | Cyclodextrin/Linoleic acid | 4,0% | Wacker-Chemie AG |
| | Parsol 1789 | Butyl Methoxydibenzoylmethane | 2,0% | Givaundan |
| | Kathon CG | Methylchloroisothiazolinone , Methylisothiazilinone | 0,1% | Rohm&Haas |
| | | | 100,0% | |

# PREPARATION OF A SUN SCREEN SOFT STICK WITH (0.30 W/W%) LINOLEIC ACID

**Calculation:**

7.4g linoleic acid are related to 100g complex, 0.296g Linoleic acid related to x g complex

$$\frac{100g \times 0.296g}{7.4g} = 4.0g$$

**Preparation:**

Heat A to approx. 60°C and mix well, add B at approx. 45°C under stirring for about 15 minutes.

The content of linoleic acid in the formulation is detected by GC.

# PREPARATION OF A SUN SCREEN SOFT GEL WITH (0.30 W/W%) LINOLEIC ACID

| Ingredients | INCI-Names | w/w | Supplier |
|---|---|---|---|
| A) Water, dd | Aqua | 86,8% | |
| CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid) | Cyclodextrin/linoleic acid | 4,0% | Wacker-Chemie AG |
| Carbopol 940 | Carbomer 940 | 2,5% | Noveon |
| Wacker Belsil® PDM 20 | Phenyl Trimethicone | 4,5% | Wacker-Chemie AG |
| Parsol MCX | Ethylhexyl Methoxycinnamate | 2,0% | Givaudan |
| Kathon CG | Methylchloroisothiazolinone, Methylisothiazilinone | 0,20% | Rohm&Haas |
| | | 100,0% | |

# PREPARATION OF A SUN SCREEN SOFT GEL WITH (0.30 W/W%) LINOLEIC ACID

**Calculation:**

7.4g linoleic acid are related to 100g complex, 0.296g Linoleic acid related to x g complex

$$\frac{100g \times 0.296g}{7.4g} = 4.0g$$

**Preparation:**

Mix all ingredients at approx. 40°C.

The content of linoleic acid in the formulation is detected by GC.

# PREPARATION OF A SUN SCREEN CREAM WITH (0.30 W/W%) LINOLEIC ACID

| | Ingredients | INCI-Names | w/w | Supplier |
|---|---|---|---|---|
| A) | Water, dd | Aqua | 60,7% | |
| | CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid) | Cyclodextrin/linoleic acid | 4,0% | Wacker-Chemie AG |
| | Carbopol 934 Polymer (1% solution) | Carbomer | 5,0% | Noveon |
| | Tetrasodium EDTA | Tetrasodium EDTA | 0,20% | |
| | Glycerine | Glycerine | 2,5% | |
| | Triethanolamine | Triethanolamine | 1,0% | |
| B) | Wacker Belsil® DM 350 | Dimethicone | 2,0% | Wacker-Chemie AG |
| | Isopropyl Myristate | Isopropyl Myristate | 9,0% | |
| | Stearyl Alkohol | Stearyl Alkohol | 9,5% | |
| | Cetyl Alkohol | Cetyl Alkohol | 0,50% | |
| | Stearic Acid | Stearic Acid | 3,0% | |
| | Sodium Stearat | Sodium Stearat | 1,0% | |
| | Parsol MCX | Ethylhexyl methoxycinnamate | 1,5% | Givaundan |
| C) | Kathon CG | Methylchloroisothiazolinone, Methylisothiazilinone | 0,10% | Rohm&Haas |
| | | | 100,0% | |

# PREPARATION OF A SUN SCREEN CREAM WITH (0.30 W/W%) LINOLEIC ACID

**Calculation:**

7.4g linoleic acid are related to 100g complex, 0.296 g linoleic acid related to x g complex

$$\frac{100\text{g} \times 0.296\ \text{g}}{7.4\ \text{g}} = 4.0\ \text{g}$$

**Preparation:**

- mix the components of phase A) at 70°C
- mix the components of phase B) at 70°C
- than pour phase A) in phase B) under intense stirring
- after cool down to 45°C add finally phase C)

The content of linoleic acid in the formulation is detected by GC as described

# PREPARATION OF A BELSIL FOUNDATION WITH (0.30 W/W%) LINOLEIC ACID

| | Ingredients | INCI-Names | w/w | Supplier |
|---|---|---|---|---|
| A) | Wacker Belsil® DM 1 plus | Dimethicone | 10,00% | Wacker-Chemie AG |
| | Wacker Belsil® CM 7026 VP | C26-28 Alkyl Methicone | 2,70% | Wacker-Chemie AG |
| | Wacker Belsil® SPG 128 VP | Cyclopentasiloxane and Caprylyl Dimethicone Ethoxy Glucoside | 11,0% | Wacker-Chemie AG |
| | Wacker Belsil® DM 5 | Cyclomethicone | 2,30% | Wacker-Chemie AG |
| | Hostacerin DGI | Polyglyceryl-2 Sesquiisostearate | 2,40% | Clariant |
| | Wacker Belsil® TMS 803 | Trimethylsiloxysilicate | 1,50% | Wacker-Chemie AG |
| B) | Mixture of ferricoxide and titaniumoxide | | 8,50% | |
| | Talc | Talc | 5,00% | Grolman |
| C) | Water, dd | Aqua | 50,2% | |
| | Sodium chloride | Sodium Chloride | 2,00% | Merck |
| | CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid) | Cyclodextrin / linoleic acid | 4,00% | Wacker-Chemie AG |
| D) | Fragrance | Perfume | 0,30% | |
| | Kathon CG | Methylchloroisothiazolinone, Methylisothiazilinone | 0,10% | Rohm&Haas |
| | | | 100,0% | |

# PREPARATION OF A BELSIL FOUNDATION WITH (0.30 W/W%) LINOLEIC ACID

**Calculation:**

7.4g linoleic acid are related to 100g complex, 0.296 g linoleic acid related to x g complex

$$\frac{100\text{g} \times 0.296\ \text{g}}{7.4\ \text{g}} = 4.0\ \text{g}$$

**Preparation:**

- mix the components of phase A) at 75°C
- mix the components of phase B) and add to A) under intense stirring
- disperse the complex in phase C) at 50°C
- than pour slowly phase C) to the mixture of phase A) and B)
- after cool down to 45°C add finally phase D)
- than stir till the mixture is homogenous

The content of linoleic acid in the formulation is detected by GC

# SUPPLEMENTS

- Page 27, 28, 29, 30, 31, 32 ,33 and 34 on 15.03 2006, adapted formulation recipe
- Page Wacker AG 27, 29, 31 ,33 on 10.08.2006, adapted formulation recipe
- Page 18 revaised
- Page 33 and 34 revaised

# CAVAMAX®W6/LINOLEIC ACID - COMPLEX

**Consumer expect just high-quality skincare products with extraordinary performance**